

REMARKS

Claim 14 has been cancelled without prejudice.

Claim 15 has been amended to recite "The solid unit oral dosage form," and to depend from claim 24." Support for this amendment is found in the specification at, for example, paragraph 2, line 10; paragraph 11, lines 1-2; paragraph 12, lines 1-3; and Examples 2-4.

Claim 17 has been amended to delete "sufficient to administer to a human adult a daily dosage", to better conform the claim to US format.

Claims 17, 21, 22, 23, 27, 33, and 34 have been amended to recite the "solid unit oral dosage form." Claims 21, 22, and 23 have also been amended to depend from claim 24. Support for these amendments is found in the specification at, for example, paragraph 2, line 10; paragraph 11, lines 1-2; paragraph 12, lines 1-3; and Examples 2-4.

Claim 24 has been amended to recite "A solid unit oral dosage form for effecting glucose tolerance and inhibiting body weight gain or adipose tissue weight gain associated with use of a PPAR γ ligand, comprising a catechin found in green tea, and a peroxisome proliferator-activated receptor gamma (PPAR γ) ligand selected from the group consisting of thiazolidinediones, ligustilide and phytanic acid, wherein the catechin and the PPAR γ ligand are present in glucose lowering amounts." Support for this amendment is found in the specification at, for example, paragraph 2, line 10; paragraph 6, lines 1-4; paragraph 10; paragraph 11, lines 1-2; paragraph 12, lines 1-3; and Examples 1-4; and in original claim 14. See *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973); and MPEP §§ 608.01(o) and (l).

Claims 25, 28, 29, and 31 have been cancelled without prejudice.

(Claim 28 was redundant, in that it was a duplicate of claim 21.)

Claim 26 has been amended to recite a "solid unit oral dosage form", and to replace "prevents" with "inhibits". Support for these amendments is found in the specification at, for example, paragraph 2, line 10; paragraph 6, lines 1-4; paragraph 10; paragraph 11, lines 1-2; paragraph 12, lines 1-3; and Examples 1-4.

Claims 30 and 32 have been amended to recite the "solid unit oral dosage form." Support for these amendments is found in the specification at, for example, paragraph 2, line 10; paragraph 11, lines 1-2; paragraph 12, lines 1-3; and Examples 2-4.

It is respectfully submitted that no new matter has been added.

We reserve the right to file one or more continuing applications.

Written Description Rejection

Claim 33 was rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. (Paper No. 0309 at 2.) The Examiner asserted that "[t]he claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." (Id.)

In making the rejection, the Examiner asserted that "[n]ew claim 33 recites the range limitations for the epigallocatechin gallate as being "in an amount "from 100 mg to 300 mg" and the PPAR γ ligand as being "in an amount of from 8 mg to 100 mg".

However, the examiner could not find adequate support for these two range limitations within the instant specification (as well as the original claims), including within the areas that Applicants point to therein for such support.” (Id. at 2-3.)

The Examiner concluded that “these two range limitations are deemed new matter as the original disclosure does not appear to provide adequate support therefore.” (Id. at 3.)

The Manual of Patent Examiner Procedure (“MPEP”) instructs that “the analysis [with respect to numerical range limitations] must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure.” MPEP 8th Ed., Revision 7, July 2008, § 2163.05 III (page 2100-183, right column, lines 1-4 under heading III.) The MPEP cites *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), in which “the ranges described in the original specification included a range of ‘25%-60%’ and specific examples of ‘36%’ and ‘50%’.” MPEP § 2163.05 III (page 2100-183, right column, lines 5-8 under heading III.) The MPEP indicates that in *Wertheim*, “a limitation to ‘between 35% and 60%’ did meet the description requirement.” (Id. at lines 13-15.)

In the present case, sufficient disclosure is present in the original application. Original claim 17 recites that (-)EGCG in the composition is present “in an amount of about 10 mg to about 2000 mg.” In paragraph 13, lines 1-3, the specification discloses that “EGCG doses may be from about 0.03 to about 30 mg/kg body weight/day, more particularly from about 0.2 to about 7 mg/kg body weight/day.” Examples 2-4 disclose solid unit oral dosage forms of EGCG and a PPAR γ ligand in the form of a soft gelatin capsule, a hard gelatin capsule, and a tablet, respectively. EGCG

is present in an amount of 300 mg (Example 2); 150 mg (Example 3); and 100 mg (Example 4).

Paragraph 17 discloses that 'typical doses [of the PPAR γ ligand] are in the range of about 1 to about 1000 mg, especially about 1 mg to about 100 mg ... for an adult human of about 70 kg body weight.' (Lines 1-9.) Paragraph 15 discloses that "[l]igustilide doses may be from about 0.01 to about 50 mg/kg body weight/day...". (Lines 1-3.) Examples 2-4 disclose solid unit oral dosage forms of EGCG and a PPAR γ ligand, as noted above. The PPAR γ ligand is present in an amount of 8 mg rosiglitazone (Example 2); 8 mg rosiglitazone (Example 3); and 15 mg pioglitazone (Example 4).

As in *Wertheim*, the disclosure supports a solid unit oral dosage form having an amount of (-)EGCG as recited in claim 33, namely 100 mg to 300 mg, and a PPAR γ ligand in an amount as recited in claim 33, namely 8 mg to 100 mg. It is submitted that one skilled in the art would consider the ranges in claim 33 to be supported by the specification.

In view of the foregoing, it is submitted that the rejection has been overcome and should be withdrawn.

Enablement Rejection

Claims 24, 26, 28, 30, and 32 were rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. (Id. at 3.)

In making the rejection, the Examiner asserted that the specification "does not reasonably provide enablement for the intended use of preventing ... body weight

gain or adipose tissue weight gain *in vivo* (including in a subject being administered a PPAR γ ligand such as the elected species - ligustilide, in combination with EGCG).”
(Id.)

The Examiner acknowledged, however, that the specification is “enabling for the intended use of treating and/or inhibiting body weight gain or adipose tissue weight gain associated with the use of a PPAR γ ligand.” (Id.)

The Examiner “suggested that the terms ‘preventing’ (claim 24, line 3) and ‘prevents’ (claim 26, line 6) be omitted from claims 24 and 26, and that these terms be replaced with the words --inhibiting-- and --inhibits--, respectively, to overcome the USC 112, first paragraph rejection...”. (Id. at 5.)

To further prosecution in the present application, claims 24 and 26 have been amended to, *inter alia*, make the amendments suggested by the Examiner.

In view of the foregoing, it is respectfully submitted that the rejection has been rendered moot. Reconsideration and withdrawal of the rejection are requested.

Anticipation Rejection

Claims 14, 15, 17, 21, 22, and 24-32 were rejected under 35 U.S.C. § 102(b) as being anticipated by Cui, CN 1120953, Derwent Abstract provided (“Cui”), with evidence provided by Ahmad et al., Nutrition Reviews, March 1999 (“Ahmad”) and Ko, *lap. 1. Pharmacol.*, 1980 (“Ko”). (Id.)

Cui has been summarized on the record.

In making the rejection, the Examiner asserted, *inter alia*, that “Cui teaches a therapeutic drink composition containing green tea (10-25%) and *Ligusticum wallichii* (5- 12%) out of 5 total ingredients as a health-benefiting drink.” (Id.)

Although we do not agree with the Examiner’s rejection, to further prosecution, claims 24 and 26 have been amended to recite “[a] solid unit oral dosage form,” claim 14 has been cancelled, and the remaining claims under consideration have been amended to depend (ultimately) from claim 24 or claim 26.

As noted in the prior Response, a proper rejection under § 102(b) requires that each and every element of a claimed invention be present in a single prior art reference as arranged in the claim. *Net Money, Inc. v. VeriSign, Inc.*, No. 2007-1565, 2008 WL 4614511, 7-11 (Fed. Cir. Oct. 20, 2008); *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978); *Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir. 1984.) Cui does not in any way disclose “a solid unit oral dosage form”, as presently claimed.

In view of the foregoing, it is submitted that the rejection has been rendered moot. Reconsideration and withdrawal of the rejection are respectfully requested.

Obviousness Rejections

A. Cui with Evidence Provided by Ahmad and Ko

Claims 14, 15, 17, 21, 22, and 24-34 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cui, “with evidence provided by” Ahmad and Ko. (Paper No. 0309 at 6.)

In making the rejection, the Examiner cited "the reasons of record". (Id.)
The Examiner then concluded that "one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention." (Id. at 8.)

The Examiner made additional assertions by way of response to prior arguments, including that "the health-benefiting drink composition taught by Cui inherently comprises a catechin such as epigallocatechin gallate (inherently contained within green tea) and ligustilide (inherently contained within *Ligusticum wallichii*) - including being present within such a composition so as to provide the broad dosage ranges of each therein - as best understood by the claim language, as drafted (e.g. "the instant claim language still does not define in a positive manner as to what such a dosage of EGCG and/or ligustilide is in relation to)." (Id. at 9.)

In addition, the Examiner asserted that with regard to prior arguments to the effect "that combinations of EGCG and rosiglitazone provide surprising unexpected results[,] the claims have been examined insofar as they read upon the elected species - i.e., EGCG and ligustilide (not rosiglitazone). Further, in terms of the broader aspect of any unexpected results achieved by the combination of EGCG and a PPAR γ ligand such as ligustilide, ... the amounts of ligustilide and EGCG instantly claimed are not defined in relative terms: i.e., with respect to being contained within a particular amount of the claimed pharmaceutical composition." (Id. at 10.)

Although we do not agree with the Examiner's rejection, to further prosecution, claims 24 and 26 have been amended to recite "[a] solid unit oral dosage form." As noted above, claim 14 has been cancelled, and the remaining claims under consideration have been amended to depend (ultimately) from claim 24 or claim 26.

Arguments submitted on the record to date are incorporated here as though presented in full.

It is submitted that the present claims satisfy the Examiner's concerns regarding the claim language. Present claims 24 and 26 recite that "the catechin and the PPAR γ ligand are present in glucose lowering amounts" and that "the effective amount of each of the catechin and the PPAR γ ligand in combination reduces fasted state glucose concentrations", respectively. Furthermore, these claims recite "[a] solid unit oral dosage form for effecting glucose tolerance and inhibiting body weight gain or adipose tissue weight gain associated with the use of a PPAR γ ligand ...", and that "the effective amount of each of the catechin and the PPAR γ ligand in combination reduces fasted state glucose concentrations and inhibits body weight gain or adipose tissue weight gain associated with the use of a PPAR γ ligand", respectively. We refer the Examiner to the arguments submitted in the prior Response regarding that the claimed invention achieves glucose tolerance with the unexpected results of minimizing the side effects of PPAR γ ligands, i.e., inhibiting body weight gain or adipose tissue weight gain associated with the use of PPAR γ ligands.

In addition, we also note that PPAR γ ligands, *e.g.*, rosiglitazone, pioglitazone, ligustilide, *etc.*, are potent treatment options for patients with type 2 diabetes. However, it is well known that such PPAR γ ligands promote adipocyte differentiation and lead to increased fat accumulation and weight gain. (See paragraph 9 of the specification.) Increased body weight and adiposity have been detected in animals and humans treated with PPAR gamma agonists. This may have a negative

impact on diabetic patients, and these effects are considered prominent adverse effects for this class of compounds.

Surprisingly, the combination of a PPAR gamma ligand and EGCG in accordance with the claimed invention inhibits the adverse effects of PPAR γ compounds seen when PPAR γ ligand-containing compounds are given alone (see, e.g., paragraphs 10, 20, 24, 34 and 35 of the specification). In the disclosed studies, the typical PPAR γ mediated side effects such as increased body weight and adiposity were prevented by supplementation with a PPAR γ ligand in combination with EGCG.

One skilled in the art would have thought that combining two compounds with two different side effect profiles would result in the addition of the side effects of the two compounds. It would not have been expected that the side effect of one of the compounds, in this case the PPAR γ ligand, would be suppressed or inhibited in the combination. Thus, the elimination or inhibition of these side effects achieved with the claimed solid unit oral dosage form is surprising and unexpected.

It is submitted that it is proper for the Examiner to consider the evidence in the specification regarding all the PPAR γ ligands disclosed and claimed, rather than merely the elected ligustilide species. The election of a species relates to the Examiner's search for prior documents, and does not limit the consideration of disclosed evidence related to the claimed PPAR γ ligands selected from the group consisting of thiazolidinediones, ligustilide, and phytanic acid, as claimed.

Cui, which discloses a health-benefiting drink which includes at least five components, neither discloses nor suggests a solid unit oral dosage form. Nor does Cui disclose or provide any expectation of success in achieving the minimization of side

effects associated with PPAR γ ligands. Moreover, Cui provides no indication of how glucose tolerance with minimization of the side effects associated with PPAR γ ligands could be achieved in a solid unit oral dosage form. Cui provides no reason for one skilled in the art to choose EGCG and a PPAR γ ligand such as ligustilide, and no indication that such unexpected results could be achieved thereby. Moreover, one skilled in the art would not look to formulate all five components of Cui's beverage in a solid unit oral dosage form because the amounts disclosed in Cui would render a solid unit oral dosage form, e.g., a tablet or capsule, too large to be administered.

In view of all of the foregoing, it is respectfully submitted that the rejection has been rendered moot.

B. Morre and Zhao

Claims 14, 15, 17, and 21-34 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Morre et al., U.S. Patent No. 6,410,061 ("Morre") and Zhao, U.S. Patent Publication 2003/0165580 ("Zhao"). (Id. at 10.)

Morre and Zhao have been summarized on the record.

In making the rejection, the Examiner cited "the reasons set forth in the previous Office action". (Id.) The Examiner concluded that "one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention." (Id. at 12.)

The Examiner made additional assertions in response to prior arguments, including that "these instantly claimed functional effects would be *intrinsic* to a composition comprising anticancer effective amounts of EGCG and ligustilide therein, as reasonably suggested by the combined teachings of the cited references - e.g.,

based upon the beneficial teachings provided by Morre et al. and Zhao including with respect to the useful anti-cancer amounts of such ingredients (each of which are within the instantly claimed amount ranges - as best understood) as disclosed therein.” (Id. at 13) (emphasis added.)

To further prosecution, the claims have been amended, as noted above.

Arguments on the record, including from the prior Response and the argument in section A above, are incorporated herein as though presented in full.

Inherency is not proper consideration under § 103. That which is inherent in the prior art, if not known at the time of the invention, cannot form a proper basis for rejecting the claimed invention as obvious. *In re Shetty*, 195 USPQ 753, 756-57 (CCPA 1977). In *Shetty*, the Court stated:

[T]he inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown. 195 USPQ at 757.

Furthermore, the court stated in *In re Naylor*, 152 USPQ 106, 108 (CCPA 1966), that “[inherency] is quite immaterial if ... one of ordinary skill in the art would not appreciate or recognize the inherent result.” The Court of Appeals for the Federal Circuit reiterated that “a retrospective view of inherency is not a substitute for some [reason] supporting an obviousness rejection.” *In re Rijckaert*, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (holding that “the burden to rebut a rejection of obviousness does not arise until a *prima facie* case has been established”).

It is respectfully submitted that the Examiner has erred in asserting that the claims are obvious because the “effects would be intrinsic...”. (Id.) As argued in

the prior Response and in Section A above, the presently claimed method achieves glucose tolerance with the unexpected result of minimization of the side effects of PPAR γ ligands, i.e., inhibiting body weight gain or adipose tissue weight gain associated with the use of a PPAR γ ligands. It is of no moment whether or not the Examiner's proposed combination of Morre, which discloses a pharmaceutical composition comprising green tea catechins to treat various cancers, and Zhao, which discloses a pharmaceutical composition of ligustilide to treat gynecological diseases including ovarian cancer, would result in the same inherent result as the claimed solid unit oral dosage form with regard to glycemic control and minimization of the side effects of PPAR γ ligands. The claimed invention achieves surprising results that were not known or expected. The Examiner's hindsight combination of documents does not suggest otherwise.

It is respectfully submitted that the rejection has been rendered moot. Reconsideration and withdrawal of the rejection are requested.

Double Patenting

Claims 14, 15, 17 and 21-34 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15-24 of copending Application No. 10/556,199 ("the '199 Application"), in view of Hara et al., U.S. Patent No. 5,318,986 ("Hara"). (Paper No. 0309 at 14.)

Hara was summarized in the prior Response.

In making the rejection, the Examiner repeated the arguments made in the prior Action. The Examiner concluded that "it would have been obvious to one of

ordinary skill in the art at the time the claimed invention was made to combine the claimed antidiabetic ligustilide pharmaceutical composition set forth in Appl. No. '199 with epigallocatechin gallate based upon the beneficial teachings provided by Hara et al. with respect to epigallocatechin gallate also being an effective anti-diabetic agent." (Id.)

The Examiner made additional assertions, including that "these instantly claimed functional effects would be intrinsic to a composition intended to effectively treat diabetes comprising EGCG and ligustilide therein." (Id. at 15.)

To forward prosecution, the claims have been amended as noted above.

The arguments provided on the record regarding the unexpected results achieved are incorporated here.

We also incorporate the arguments presented in section B above in reply to the § 103 rejection over Morre and Zhao. In particular, as noted above, that which is inherent in the prior art, if not known at the time of the invention, cannot form a proper basis for rejecting the claimed invention as obvious. *In re Shetty*, 195 USPQ at 756-57. Because a provisional double patenting rejection applies a § 103 analysis, it is improper for the Examiner to assert that the claims are obvious over the '199 Application in view of Hara because the "effects would be intrinsic...".

As noted, the presently claimed method achieves glucose tolerance with the unexpected result of minimization of the side effects of PPAR γ ligands, i.e., inhibiting body weight gain or adipose tissue weight gain associated with the use of a PPAR γ ligands. It is of no moment whether or not the Examiner's proposed combination of the '199 Application, and Hara, which discloses the use of a composition

of EGCG from green tea for treating diabetes, would result in the same inherent result as the claimed solid unit oral dosage form with regard to glycemic control *and* minimization of the side effects of PPAR γ ligands. The claimed invention achieves surprising results that were not known or expected. The Examiner's hindsight combination of documents does not suggest otherwise.

It is respectfully submitted that the rejection has been rendered moot. Reconsideration and withdrawal of the rejection are requested.


Therefore, for the reasons set forth above, entry of the amendments, withdrawal of the rejections, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, June 22, 2009.



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